CSPI CENTER FOR SCIENCE IN THE PUBLIC INTEREST
Publisher of *Nutrition Action Healthletter*

July 17, 2000

Dr. Jane Henney
Commissioner
Food and Drug Administration
5600 Fischer Lane
Rockville, MD 20857

Re: Petition to Set A Regulatory Limit for Methylmercury In Seafood That Reflects the Risk to Pregnant Women and Children From the Intake of Seafood Containing Methylmercury

Dear Commissioner Henney:

More than 60,000 children are born each year at risk for neurological problems due to low-level methylmercury contamination from seafood eaten by pregnant women, according to a National Academy of Sciences (NAS) report released last week.[1] This warning is not new. Concerns about the effects of this toxic metal on pregnant women and their fetuses were raised nearly a decade ago, in a 1991 NAS report and in a citizen petition I submitted to the Food and Drug Administration (FDA) in 1992. Both the report and the petition were highly critical of the FDA's weak standard on methylmercury in seafood[2] and offered the agency specific guidance on performing a more rigorous risk assessment on the substance. Unfortunately, the FDA has never revised its methylmercury action level or responded to the petition. It is imperative that the agency act without further delay. On behalf of the Center for Science in the Public Interest (CSPI), I am resubmitting the attached petition urging the agency to set a regulatory limit for methylmercury in fish and shellfish that protects pregnant women and children from mercury contamination.

As in the earlier NAS report, several of the panel's recommendations, when applied to the FDA's guidelines on methylmercury, reveal fatal flaws in the agency's standard-setting process. Most importantly, the 2000 NAS panel validated the EPA's stringent regulatory limit for

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[1] National Academy of Sciences, Toxicological Effects of Methylmercury, 276 (not yet published), found at *http://www.nap.edu/openbook/0309071402/html/276.html* [hereinafter cited as 2000 NAS report].

[2] The FDA's action level for methylmercury is 1 part per million (ppm).

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methylmercury,[3] but when the data used in FDA's risk assessment are plugged into the model, **the FDA's biomarker and exposure levels for methylmercury are four times higher than the NAS endorses.**[4] Specifically, the 2000 NAS panel found the following:

1. There is a "strong data base" of human and animal studies showing neurotoxic effects from in utero exposure to methylmercury and particularly the 1997 Faroe Islands study[5] on the effects of low-level chronic exposure.[6] *The FDA action level is based upon a 1971 study of two high-exposure poisoning episodes occurring in the 1960's. Although the FDA conceded in 1994 that long-term exposure to methylmercury in fetuses and infants might have adverse harm,[7] the agency did not reevaluate its action level when the Faroe Islands, Seychelles (1998) or New Zealand (1986, 1989) studies on developmental neurotoxicity were released.*[8]

2. Developmental neurotoxicity should be the end point used in calculating the appropriate regulatory level of methylmercury.[9] *The FDA used overt neurological symptoms in adults as the end point; therefore its action level is set to protect adult men weighing 154 pounds and over.*

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[3] Id. at 277, found at *http://www.nap.edu/openbook/0309071402/html/277.html.* The 2000 NAS report was issued following an 18-month review of the toxicological effects of methylmercury and the validity of the EPA's risk assessment on the substance. As part of its work, the panel of scientists analyzed the data and assumptions used by FDA, EPA and other agencies. Id. at 257, found at *http://www.nap.edu/openbook/0309071402/html/277.html.*

[4] Id. at 17, 277, found at *http://www.nap.edu/openbook/0309071402/html/17.html, http://www.nap.edu/openbook/0309071402/html/277.html.* The FDA's action level for methylmercury is based upon a biomarker in adult blood of 0.2 ppm (or a concentration of 0.02 μg/g of blood, including a safety factor of ten, which equates to 20μg/L of blood). Removing the safety factor leaves a blood concentration of 200 μg/L of blood, and applying the 250:1 blood:hair ratio results in 50 ppm in hair.

[5] See, 2000 NAS report at Chapter 6: Comparison of Studies for Use in Risk Assessment at 209-226, found at *http://www.nap.edu/openbook/0309071402/html/209.html - http://www.nap.edu/openbook/0309071402/html/226.html* for a discussion of the Faroe Islands study as well as the Seychelles and New Zealand studies on exposure to methylmercury and developmental neurotoxicity.

[6] 2000 NAS report at 275, found at *http://www.nap.edu/openbook/0309071402/html/275.html.*

[7] FDA, Mercury in Fish: Cause for Concern?, FDA Consumer (Sept. 1994, rev'd. May 1995).

[8] See, *supra*, note 5.

[9] 2000 NAS report at 275, found at *http://www.nap.edu/openbook/0309071402/html/275.html.*

3. The risk assessment should be based upon a benchmark dose limit (BMDL)[10] corresponding to 12 ppm in hair.[11] *The FDA action level corresponds to a biomarker of 50 ppm in hair, which is more than 4 times the NAS recommendation.*

4. A regulatory limit for methylmercury of 0.1 μg/kg/day–the EPA standard–is "scientifically justifiable for the protection of public health."[12] *The FDA's action level is equivalent to 0.4 μg/kg/day.*

The NAS report adds to the large body of science showing the adverse effects of low-level methylmercury exposure on developing fetuses and documents that 60,000 children are born each year at risk of developing neurological problems from mercury exposure linked to seafood. It is imperative that FDA act now to protect women of child-bearing age and their children from this hazard. First, FDA should immediately adopt EPA's standard for methylmercury as an "action level." Second, FDA should monitor methylmercury levels in shark, swordfish and tuna and remove seafood from the market that violates FDA's standard. Third, FDA should act on the attached 1992 petition by initiating rulemaking to adopt a tolerance for methylmercury that fully protects the children of women who are or may become pregnant. Further delay by the agency would be unconscionable.

Sincerely,

Caroline Smith DeWaal

Caroline Smith DeWaal
Food Safety Director

Encl.

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[10] "Benchmark dose" (BMD) refers to the estimated dose that corresponds to a specified risk above the background risk. BMDL denotes the corresponding lower limit. Id. at 228, found at *http://www.nap.edu/openbook/0309071402/html/228.html.* For example, the benchmark dose of 11 ppm of mercury in hair was calculated as the 95% lower confidence limit on the maternal-hair concentration corresponding to a 10% extra risk level. The lower confidence limit is the BMDL. Id. at 258, found at *http://www.nap.edu/openbook/0309071402/html/258.html.*

[11] Id. at 277, found at *http://www.nap.edu/openbook/0309071402/html/277.html.* The NAS determined that the BMDL used by EPA (11 ppm) is "nearly identical" to the panel's recommendation of 12 ppm in hair. Id.

[12] Id. at 277, found at *http://www.nap.edu/openbook/0309071402/html/277.html.* The 2000 NAS report was issued following an 18-month review of the toxicological effects of methylmercury and the validity of the EPA's risk assessment on the substance. As part of its work, the panel of scientists analyzed the data and assumptions used by FDA, EPA and other agencies. Id. at 257, found at *http://www.nap.edu/openbook/0309071402/html/277.html.* The panel's findings reveal serious defects in the methods and data that FDA used in determining its action level for methylmercury.

THE U.S.DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Petition to Set a Regulatory Limit for Methylmercury in Seafood that Reflects the Risk to Pregnant Women and Children From the Intake of Seafood Containing Methylmercury	Docket No. _____

Submitted by

Public Voice for Food and Health Policy

April 7, 1992

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EXECUTIVE SUMMARY

Public Voice for Food and Health Policy submits this petition to request the FDA to set a regulatory limit for methylmercury in fish and shellfish to replace the present action level. This regulatory limit should reflect the well-documented effects of dietary exposure to methylmercury on pregnant women and children.

Large ocean dwelling fish, such as tuna, swordfish, shark, and halibut, and some fresh water fish concentrate methylmercury in their bodies at levels of concern to humans. The risks of methylmercury exposure grow as consumers purchase more seafood seeking a lower fat source of protein. Per capita consumption of seafood increased 24% between 1980 and 1990. Seafood containing mercury are very popular: swordfish and tuna are common menu items and canned tuna is likely the most commonly consumed form of seafood. In 1990, canned tuna accounted for 23.9% of seafood consumption.

The toxic effects of methylmercury in the diet have been extensively documented over the last 30 years. In Minamata, Japan, the children of women who consumed methylmercury in fish were found to suffer long term effects, following a poisoning episode in the late 1950's. Additional findings followed a poisoning episode in Iraq in the 1970's.

Although the FDA first recognized the health threat that mercury in fish posed when it developed a regulatory guideline for methylmercury in 1969, the agency admits that the guideline

is not sufficient to protect women of childbearing age from accumulating quantities of mercury in their bodies which could pose a threat to the health of their children. Despite this admission, the agency relaxed the standard for methylmercury in fish and shellfish based on economic considerations that benefit the industry.

In its 1991 report Seafood Safety, the National Academy of Sciences (NAS) criticized the FDA's current 1.0 ppm action level for methylmercury in fish and shellfish. The NAS concluded that the adequacy of the current standard to protect the fetus is highly doubtful. The report recommended that in canned tuna products, "much lower levels of mercury [than the current government-approved levels] should be maintained" to protect babies and young children.

Methylmercury in fish and shellfish is presently regulated by an action level that is not legally enforceable rather than a regulatory limit. This action level serves only as an informal guideline for the industry of when the agency might take action. A regulatory limit for methylmercury would be legally enforceable and therefore it is much more effective. It is binding on the agency and the industry, providing greater protection for consumers. It would eliminate the need for the FDA to reprove the threat to public health every time it goes to court to remove seafood that violates the standard. In setting the regulatory limit, the FDA must consider the effect of methylmercury exposure on pregnant women and children.

April 7, 1992

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 4-62
5600 Fishers Lane
Rockville, MD 20857

Public Voice for Food and Health Policy submits this petition under 21 U.S.C. § 331 and 21 U.S.C. § 342(a)(1) of the Federal Food, Drug, and Cosmetic Act[1] and 21 C.F.R. § 109.4 and 21 C.F.R. § 109.6[2] to request the Commissioner of Food and Drugs to issue a regulation setting a regulatory limit for methylmercury residues in seafood that fully protects pregnant women and their children from the adverse human health effects associated with methylmercury exposure.

A. Action Requested

Public Voice respectfully requests that the FDA immediately initiate a rulemaking procedure to set a regulatory limit for methylmercury in fish and shellfish and to request the submission of information from the scientific community within three months on the appropriate level for that regulatory limit, based on full

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[1] Federal Food, Drug and Cosmetic Act of 1938, § 301, § 402(a), 21 U.S.C. § 331, § 342(a) (1988).

[2] 21 C.F.R. § 109.4, § 109.6 (1991).

consideration of the effects that methylmercury and mercury have on adults, children and the offspring of women that are exposed to it through their diet.

B. Statement of Grounds

I. INTRODUCTION

The toxic effects of methylmercury in the diet were extensively documented following several mass poisoning episodes, including a 1956 incident in Minamata, Japan, where the source of methylmercury was fish and a 1972 incident in Iraq, where the source of methylmercury was contaminated wheat. Mercury, particularly in the methylated form common in seafood, can cause deafness, blindness, coordination problems, tremors, mental disturbance, congenital defects and even death.[3] The FDA used evidence about the toxic properties of mercury derived from these episodes to set a standard for the permissible level of mercury and methylmercury in seafood. However, the FDA has set this standard based on evidence about the acute effects that methylmercury has in adults, without making allowance for the needs of sensitive groups such as pregnant women and children.

Seafood is a well-recognized source of exposure to methylmercury.[4] Mercury is ubiquitous in the marine environment.

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[3] Harada, Minamata Disease: Chronology and Medical Report, in Minamata: Words and Photographs 59-62 (W. Smith, A. Smith 1975) [hereinafter "Harada"]; 39 Fed. Reg. 42,738 (1974).

[4] 39 Fed. Reg. 42,738 (1974). Methylmercury is the most

Significant amounts of mercury in the environment result from human uses, such as agriculture and industry. In water, mercury is converted to methylmercury, the most toxic form, by microorganisms in sediment and is concentrated in the tissue of fish and other aquatic species.[5]

Predatory fish that live a long time, such as tuna, swordfish, shark, halibut and some fresh water fish, are known to concentrate methylmercury at high levels. These fish bioaccumulate methylmercury from the organisms that make up their diet and from the water column. Methylmercury is eliminated from fish very slowly, over several years, and therefore, it accumulates to levels of concern for humans.[6] Recent studies have documented methylmercury in seafood at levels that exceed even the current federal policy guideline for methylmercury.[7]

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chronically toxic form of mercury and most mercury in fish has been converted to this form, according to the FDA. Since 1984, the FDA has regulated only methylmercury in fish products. In setting a regulatory limit for methylmercury, the FDA should consider mercury exposure from all sources.

[5] 39 Fed. Reg. 42,738 (1974).

[6] 39 Fed. Reg. 42,738 (1974).

[7] Mercury in Shark Prompts Minnesota Consumer Advisory, Food Chemical News, Dec. 23, 1991 at 37 (24 of 39 samples of shark taken from Minnesota food establishments were found to exceed the federal guideline); What Else is in Fish, Consumer Reports, Feb. 1992 at 112, 114 (a test of store-bought fish found that 90% of the swordfish had detectable levels of mercury, with the average in excess of the federal guideline). The National Academy of Sciences: "Swordfish can routinely achieve even higher concentrations than the official 1-ppm guideline (which reportedly is not enforced in Massachusetts and perhaps elsewhere)." Committee on Evaluation of the Safety of Fishery Products, Food and Nutrition Board, Institute of Medicine, National Academy of Sciences, Seafood Safety 238 (1991) [hereafter Seafood Safety].

When humans consume contaminated fish, they are exposed to methylmercury and they in turn concentrate it from all sources. The chain of exposure from fish to humans led to overt mercury poisoning in the Minamata areas of Japan in the 1950's. A factory in Minamata dumped mercury into the Minamata Bay as a byproduct of acetaldehyde production. Starting in the 1950's, fish and birds were found floating in the bay and animals, such as cats, pigs and dogs, became ill and died. The first human case of Minamata Disease was identified in April 1956. By that summer, the outbreak reached "epidemic" proportions. Although the cause was identified as heavy metal poisoning from consumption of contaminated fish in 1956, the agent, mercury, was not proven until 1962. As of 1974, 798 patients were officially verified as having Minamata Disease, 107 of whom had died, and an additional 2800 people were applying for verification.[8]

The FDA should promulgate a regulatory limit for methylmercury. Despite its well-documented public health effects, methylmercury in seafood is regulated by an informal policy guideline, known as an action level, that is not legally enforceable. Each time the FDA wants to remove seafood from the market that exceeds the current action level, it must prove to a court that food exceeding the action level is a threat to the public health. Instead of this burdensome process, the FDA could establish a regulatory limit by rulemaking procedure that would establish a legal standard protective of the public health and

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[8] Harada at 55-56, 66.

would eliminate the need to prove the adequacy of the standard every time it goes to court. This would substantially shorten the time necessary to remove violative seafood from the market.

The FDA should set a regulatory limit lower than the present action level. The current action level was set to prevent overt symptoms of mercury poisoning in adult men weighing 154 lbs and over. This level is too high to protect vulnerable subpopulations. Instead, the FDA should consider methylmercury's effects on pregnant women, their offspring and children and set a limit that fully protects all humans.

II. THE FDA'S ACTION LEVEL DOES NOT FULLY CONSIDER METHYL-MERCURY'S POTENTIAL RISK FOR PREGNANT WOMEN AND CHILDREN

Methylmercury is Associated with Adverse Fetal Effects

At the 1991 National Academy of Sciences Symposium on Issues in Seafood Safety, Professor Bruce Fowler from the University of Maryland presented a paper identifying several groups as being populations of special concern in setting standards for chemical contaminants: pregnant women and infants, the aged and those suffering from malnutrition.[9] These populations require greater protection from chemicals than the average person to avoid the risk of adverse effects. However, the FDA does not take into

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[9] Fowler, Risk with Organic Contaminants in Seafood, in Proceedings of a Symposium on Issues in Seafood Safety 155 (1991) [hereinafter Seafood Safety Symposium].

consideration the heightened vulnerability of these populations when setting limits for chemical residues in fish and shellfish.

The General Accounting Office (GAO) reported that a consensus exists in the scientific community that mercury causes adverse reproductive and developmental effects.[10] Methylated mercury passes the placental barrier and targets the nervous system of the fetus.[11] It can affect normal neuronal development, leading to decreased brain size. It may also affect cell division during critical stages of development.[12]

The National Academy of Sciences' (hereafter NAS) analysis of mercury in its 1991 report Seafood Safety indicated that there may be an "appreciable" risk of developmental effects from fetal exposures to even low doses of methylmercury.[13] Based on a review of the relationship of clinical signs in humans to blood, hair, and urine mercury levels, the NAS concluded that children of symptom-free pregnant and nursing mothers with relatively low blood and hair levels may suffer from mental retardation.[14] Other symptoms of mercury poisoning in infants include cerebral palsy, delayed motor activity, delayed speech, and seizures.

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[10] United States General Accounting Office, Reproductive and Developmental Toxicants: Regulatory Actions Provide Uncertain Protection 28, 33 (1991) [hereinafter "GAO Report"].

[11] Seafood Safety at 117.

[12] World Health Organization Task Group on Environmental Health Criteria for Methylmercury, Environmental Health Criteria 101: Methylmercury at 15-16, § 1.7 (1991).

[13] Seafood Safety at 252.

[14] Seafood Safety at 117.

In Minamata, Japan, there were many findings of chronic effects and developmental effects in children. Congenital effects followed a spectrum of severity depending on dosage:

> In the schematic view of Minamata Disease, if the mother's methylmercury intake is so great that she falls acutely ill . . ., she does not become pregnant. If the dosage is somewhat less, the woman becomes pregnant but the child is spontaneously aborted or is born dead. If the dosage is even less, a child with congenital Minamata, accompanied by severe neurological symptoms, is born. Even in such cases, the mother's own symptoms may be relatively light. If the mother's mercury dosage is even less, there is a chance that the child -- even with no remarkable neurological symptoms -- may be mentally deficient. In such cases the mother may have almost no neurological symptoms.[15]

Follow-up studies of children born in the Minamata area during the period before mercury was extracted from the pollution entering Minamata Bay demonstrated dramatically the problem of fetal exposure. In a 1962 study of children born between 1955 and 1959, mental deficiency was found in 29% of the cases, substantially higher than in the control area.[16] In a 1970 study of 223 junior high school students born between 1955 and 1958 in the Minamata area, 18% were found to have mental deficiency, 21% experienced sensory disturbance, 12% had clumsy speech, and 9% had clumsy movements. These 1970 findings in the Minamata area

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[15] Harada at 67.

[16] Harada at 67, citing Harada, 66 Psychiat. Neurol. Japan 429 (1964). These results excluded the recognized congenital cases of Minamata Disease.

were substantially higher than the incidence of these conditions in other areas of Japan.[17]

Although the levels of poisoning reported in Minamata are much greater than anything that we have seen in the United States, the levels of exposure in this country are not insignificant.[18] The NAS Report Seafood Safety raises significant questions about whether the current FDA action level is adequate to protect sensitive groups:

> "Canned tuna must fall below the FDA action levels [for methylmercury]. For most consumers this is probably safe, but there are some questions in relation to sensitive groups such as babies and young children. Thus in tuna products targeted for these groups, much lower levels of mercury should be maintained.[19]

The inadequacy of the current action level for methylmercury for protecting pregnant women and children against the types of effects documented in Minamata must be addressed when establishing a regulatory limit.

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[17] Harada at 67-68. These findings were based on studies of the general population and excluded the recognized congenital cases of Minamata Disease. The examinations in the 1970 study were conducted by qualified neuropsychiatrists who directly examined the children. Harada noted that mental deficiency among junior high school children is considered to be 9.7% in Japan.

[18] The daily dose of mercury of someone who is eating 15 pounds of seafood per year was estimated by the NAS to be 2.09 micrograms per day. Seafood Safety at 237. Per capita consumption of seafood in 1990 was 15.5 lbs, an amount equivalent to one half pound serving of seafood every two weeks. Many people, particularly those seeking a healthy lower fat diet, consume more than this average amount.

[19] Seafood Safety at 329. Pregnant women are also identified as at-risk consumers by the NAS. Seafood Safety at 330.

Federal Action to Regulate Mercury Failed to Consider the Effects on Pregnant Women and Children

The FDA first set an action level for mercury in fish and shellfish in 1969. The agency set the permissible level of mercury in fish and shellfish at 0.5 parts per million (ppm), which was raised in 1979 to 1.0 ppm, the current standard. Although methylmercury is the form of mercury most toxic to humans, according to the FDA, until the 1980's there was no analytical procedure suitable for regulatory use that was capable of measuring levels of methylmercury.

In 1974, the FDA reconsidered and reaffirmed the 0.5 ppm tolerance. The FDA's decision, published in the Federal Register on December 6, 1974, recognized the unique risk to pregnant women and their children:

> Methylmercury readily crosses the placental barrier in pregnant women and enters the fetus. It may concentrate in the central nervous system of the developing organism resulting in serious brain damage to the unborn child. Fetal damage may occur at exposure levels lower than that required to produce observable effects in the mother. Therefore, chronic exposure to fish and shellfish containing methylmercury poses a greater potential for danger to women of childbearing age than to the general population.[20]

But in approving the 0.5 ppm standard, the FDA's analysis failed to make adjustments to account for these increased risks.

Using data from the poisoning episodes in Minamata Bay and Niigata, Japan and studies from Scandinavia, the FDA determined

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[20] 39 Fed. Reg. 42,738 (1974).

that the lowest whole blood concentration at which toxic symptoms occurred in adults was 0.2 micrograms per gram. This level could be reached with a daily intake of 0.3 milligrams for a 70 kilogram man. Using these data, the FDA applied a safety factor of 10 to come up with a 0.02 microgram/gram acceptable blood concentration level and daily intake of 0.03 mg for a 70 kg man.[21] According to the FDA, "[i]f fish containing 0.5 ppm mercury were eaten daily, the acceptable limit (0.03 mg) would be reached by the daily consumption of 60 grams of fish." It continued, "the average consumption of fish and shellfish in this country is regarded as considerably less than 60 grams per day."[22]

The FDA also concluded that setting a tolerance was inappropriate at that time because a study of data from the Iraqi poisoning episode was not complete.[23]

In 1979, the FDA considered the mercury action level again and recognized the lack of protection offered by its 1974 action level. In its decision, published in the Federal Register on January 19, 1979, the FDA cited the following weaknesses in the

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[21] This is the normal safety factor applied to set a tolerance for a toxic substance when the underlying data show no observable effects in human subjects. If the data show no observable effects in animal studies, a safety factor of at least 100 is applied.

[22] 39 Fed. Reg. 42,738, 42,739 (1974). Sixty grams per day is approximately one pound of seafood per week.

[23] In 1972, Iraqi farmers and their families were exposed to high levels of methylmercury from homemade bread prepared with seed wheat treated with a fungicide containing methylmercury.

original approach to setting the 0.5 ppm action level for mercury:

> (1) it was not known to what extent particular individuals are more or less sensitive to mercury than others; (2) the estimates were based on the "lowest level that caused an effect" rather than the normal procedure of using a "no effect dose level"; **(3) questions about dose/response relationships in human fetuses and newborn infants were unanswered;** and (4) there is a possibility of subclinical effects arising from exposure to very low levels of methylmercury.[24] (emphasis added)

Instead of strengthening the action level to account for these weaknesses in the original standard setting, FDA relaxed it to 1.0 ppm on the basis of new consumption information and socioeconomic impacts presented to it by the National Marine Fisheries Service (NMFS).[25] According to the FDA:

> The NMFS concluded that a 1.0 ppm action level would protect consumers as much as does the 0.5 ppm level. Also, the higher level would provide a significant economic benefit to those industries most seriously affected by regulatory actions under the 0.5 ppm guideline and would enhance the future development of a number of presently underutilized fisheries. The report also stated that the less restrictive regulatory approach it recommended would significantly increase consumer confidence in seafood.[26]

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[24] 44 Fed. Reg. 3,990, 3,992 (1979).

[25] The consumption data used to justify increasing the action level to 1 ppm from 0.5 ppm in 1979 is clearly out of date, as consumption has increased 24% from 1980 to 1990. According to NMFS officials, the agency has no intention of producing an updated consumption survey to reanalyze mercury exposure.

[26] 44 Fed. Reg. 3,990, 3,992 (1979). Action levels and regulatory limits are set pursuant to FDA's authority under § 342(a)(1), which states that food is adulterated when it contains

The FDA also commented that it would continue to regulate mercury with an action level rather than a tolerance because "FDA expects to continue to receive new information bearing on the appropriate limit for mercury in fish and other aquatic animals."[27]

In 1984, the FDA revised the 1.0 ppm action level so that it applied only to methylmercury. The Association of Official Analytical Chemists published an analytical method for methylmercury that was suitable for enforcement purposes. In the decision published in the Federal Register on November 19, 1984, the FDA said:

> The agency acknowledges that the revision of the action level might result in a slight increase in consumer exposure to methyl mercury [sic]. However, this increase in exposure will not be of public health concern.[28]

Despite the recognition by the FDA in 1974 that exposure to methylmercury resulted in a possibility of fetal effects, no allowance was made in setting the action level to provide protection for pregnant women and children.[29] Later decisions in 1979 and 1984 that increased exposure to mercury never revisited

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a substance "which may render it injurious to health." There is no basis for the consideration of the economic consequences and "consumer confidence" employed here under this section.

[27] 44 Fed. Reg. 3990 (1979).

[28] 49 Fed. Reg. 45,663 (1984).

[29] GAO Report at 58.

the issue of fetal effects.[30] Now, with over 30 years of data documenting these effects since the original mass poisoning at Minamata, Japan, the FDA should set a regulatory limit for methylmercury in seafood that fully considers the issue of fetal sensitivity, and fully protects pregnant women and children from potential harm from methylmercury exposure.

The NAS Criticized the FDA's Methylmercury Standard for Not Adequately Protecting Pregnant Women and Children

Seafood Safety extensively criticized the FDA's analysis in setting its 1.0 ppm action level for methylmercury.[31] Not surprisingly, this criticism identifies many of the same weaknesses that the FDA recognized in 1979 when it reexamined the toxicological data on the 0.5 ppm standard. In addition, Seafood Safety demonstrates that Iraqi data now allow quantitative estimates to be made of the apparent degree of human interindividual variability in susceptibility and the protectiveness of the traditional ten-fold safety factor for both adults and developing fetuses. Their analysis concludes that the

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[30] Staff of the FDA have admitted that there is data from the Iraqi poisoning episode showing effects on children at exposure levels similar to those found in the U.S. but that they consider the data inadequate to base a regulatory decision because there are only "four data points." (Conversations with FDA staff on March 18 and 19, 1992.)

[31] At the National Academy of Sciences Symposium on Issues in Seafood Safety, Dale Hattis, the author of Seafood Safety's section on risk assessment and methylmercury, observed that there was no recognition among the FDA staff charged with setting standards for chemical contaminants in seafood that they had a problem in assessing non-cancer risks. Seafood Safety Symposium at 75.

adequacy of the ten-fold factor for the fetus is highly doubtful.[32]

In setting regulatory limits and action levels, it is common practice for the FDA to identify a level where no effects are observed (NOEL) or where no adverse effects are observed (NOAEL) in studies with either human or animal subjects, and then apply a multiple of 10, if the data are derived from human exposure, or 100, if the data are derived from animal exposure.[33] The human "safety factor" of 10 is used to account for individual differences in sensitivity. The animal factor of 100 accounts for the additional sensitivity that may arise across species.[34]

The FDA varied from this practice in setting the standard for mercury by using the lowest level of mercury exposure where an effect was observed and applying a 10-fold safety factor. The NAS characterized as unusual the fact that the FDA used the lowest level that caused an effect (LOEL) rather than the no observable effect level (NOEL), that is typically used. According to the NAS:

> For mercury, the likely special susceptibility of developing fetuses was mentioned in discussion. However, a tenfold "safety factor" was applied to the lowest blood level reported to produce effects for adults (rather than to a no-effect level of

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[32] Seafood Safety at 196-211.

[33] Seafood Safety at 176-7.

[34] If data are derived from a LOEL (lowest observable effects level) in animals, an additional safety factor of 10 is applied, making the total safety factor 1000. D.G. Barnes, M. Dourson, "Reference Dose: Description and Use in Health Risk Assessments," Regulatory Toxicology and Pharmacology 476 (1988).

> intake, which would have been more consistent with established procedures) in the cited epidemiological studies, without numerical allowance for the extra sensitivity of fetuses . . . .[35] (emphasis in original)

The fact that the FDA failed to make allowance for the sensitivity of the fetus is not in dispute. According to the 1991 GAO report Reproductive and Developmental Toxicants: Regulatory Actions Provide Uncertain Protections, the FDA reported to the GAO that it failed to examine data on mercury's reproductive and developmental toxicity when it weakened the action level from 0.5 ppm to 1 ppm.[36]

In addition, the FDA failed to make allowance for two critical variables in setting the action level for mercury. First, there are well-documented differences among individuals in their rate of mercury elimination. A study of the biological half-life[37] of mercury in individuals exposed in the Iraqi poisoning episode reported a range of between 37 days and 189 days.[38] Second, fetuses showed greater variability than adults in their response to mercury exposure. According to the NAS report, the "interindividual variability in susceptibility for fetal

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[35] Seafood Safety at 187.

[36] GAO Report at 58.

[37] The "half-life" of a chemical is the period of time for a chemical concentration in a specific medium to decrease by 50% from its original concentration.

[38] Seafood Safety at 198. In one study of the autopsy results from victims of Minamata Disease, the biological half-life of methylmercury in the brain was found to be 230 days. Harada at 68-69, citing Takeuchi, Epidemiological, Clinical and Pathological Studies on Minamata Disease Ten Years After the Outbreak (1973).

effects is much broader than that for adult effects."[39] Because of this, fetuses may have greater risk at low doses. The NAS report concluded, "although the tenfold safety factor, as applied, appears to offer a reasonable degree of protection for adult effects, projections . . . of the fetal dose-response data suggest the possibility of appreciable risk from methylmercury exposure, even at levels to which many people are exposed via the diet."[40]

The use of a "lowest observable effects level," and the additional uncertainties of individual variability and greater fetal susceptibility strongly suggest that the use of a safety factor of 10 by the FDA was inappropriate. A substantially higher safety factor should have been used. The present action level of 1.0 ppm does not adequately protect pregnant women, their offspring and children from the potential adverse effects associated with methylmercury consumption and should be replaced with a regulatory limit set well below 1.0 ppm.

III. THE FDA HAS THE AUTHORITY TO SET A REGULATORY LIMIT FOR METHYLMERCURY IN SEAFOOD BUT HAS NOT DONE SO

A Regulatory Limit is Needed Because an Action Level Cannot Adequately Protect Consumers

The FDA is responsible for assuring that adulterated food does not come to the market. A food is deemed to be adulterated when it contains "any [added] poisonous or deleterious substance

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[39] Seafood Safety at 188.

[40] Seafood Safety at 188.

which may render it injurious to health . . ."[41] An "added" substance is one that has been introduced artificially or is attributable to some degree to the acts of man.[42] So long as any portion of a substance present in food is attributable to the acts of humans, all of that substance will be considered "added."[43]

The presence of mercury in fish is to some extent due to human acts. Fish and shellfish take in methylmercury from seawater, and from the aquatic animals upon which they feed. The FDA has determined that "significant amounts of mercury enter the (aquatic) environment from man's agricultural and industrial use. . ." [44] Since at least part of the mercury found in seafood is attributable to the acts of humans, mercury is "added" to seafood under the court decision in U.S. v. Anderson Seafoods, Inc.

The Federal Food, Drug and Cosmetic Act (FFDCA) sets forth several approaches the FDA can use to regulate food containing harmful substances in the market. First, if the FDA discovers an adulterated food through its monitoring and enforcement

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[41] 21 U.S.C. §342(a)(1) (1988). The section contains a separate clause governing foods with substances that are not added, which makes clear the quoted section governs only foods with added substances.

[42] U.S. v. Anderson Seafoods, Inc., 447 F.Supp. 1151, 1155 (N.D. Fla. 1978), aff'd, 622 F.2d 157 (5th Cir. 1980).

[43] U.S. v. Anderson Seafoods, Inc., 622 F.2d 157, 161 (5th Cir. 1980). Other courts have followed the Anderson rule: Continental Seafoods, Inc. v. Schweiker, 674 F.2d 38 (D.C. Cir. 1982); Seabrook International Foods, Inc. v. Harris, 501 F.Supp. 1086 (D.D.C. 1980).

[44] 39 Fed. Reg. 42,738 (1974).

activities, the FDA can initiate proceedings in court to prohibit the introduction or delivery of the food into interstate commerce.[45] The FDA may do this by directly initiating seizure or injunction proceedings in the U.S. District Courts, or by recommending criminal prosecution to the Justice Department.[46]

Alternatively, the FDA can promulgate a regulatory limit for a harmful or added deleterious substance under 21 U.S.C. §342(a)(1).[47] A regulatory limit may be promulgated when a poisonous or deleterious substance cannot be avoided in a food product, as is the case with mercury in seafood.[48] A regulatory limit represents the bright line between food considered safe and food considered adulterated under the FDA's general enforcement authority.[49]

Regulatory limits are binding on the FDA and the industry. There is no need for the FDA to prove that the food is adulterated in a seizure or an injunction proceeding in court. Instead, the only issue is whether the regulatory standard was exceeded.

Action levels, on the other hand, are mere policy statements that give industry notice of when the FDA may act to prohibit

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[45] 21 U.S.C. § 331(a) (1988).

[46] Telephone interview with Donna Lenahan, FDA Office of Legislative Affairs (Feb. 4, 1992). This general enforcement authority is granted to FDA under 21 U.S.C. § 342(a).

[47] 21 U.S.C. § 342(a)(1) (1988).

[48] 21 C.F.R. § 109.6(c) (1991).

[49] 21 U.S.C. § 342(a)(1) (1988).

food from going to the market. They simply provide non-binding guidelines for when the FDA may recommend court proceedings in its prosecutorial discretion against a food under the FDA's general enforcement authority.[50] Because of their unenforceability, action levels provide no real benefit to consumers.

Regulating methylmercury through a regulatory limit is preferable to continued regulation through the FDA's general enforcement authority and the existing action level for two reasons. First, a regulatory limit would be binding on both the industry and the FDA whereas the present action level is not. Under a regulatory limit, if the amount of methylmercury in a shipment of fish exceeded the allowable level, the courts would be required to exclude fish from the market. The FDA's discretion as to whether or not to attempt to suppress the fish from the market would be eliminated. The FDA would be bound to enforce the regulatory limit, and the industry would know in advance that a methylmercury level above the regulatory limit would not be allowed on the market.[51]

This gives consumers more uniform protection. They will know that whenever they eat fish tested by the FDA, its methylmercury content will not exceed a certain level. "Once binding regulations are promulgated, the industry and public are

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[50] Community Nutrition Institute v. Young, 818 F.2d 943, 949 (D.C. Cir. 1987).

[51] 55 Fed. Reg. 29782, 29783.

put on notice and may be guided accordingly rather than speculate as to the outcome of a seizure or enforcement suit."[52]

Second, a regulatory limit would allow the FDA to regulate the level of methylmercury in seafood without having to return repeatedly to court to prove that fish is "adulterated" within the meaning of §342(a). This conserves agency and judicial resources, maintains a uniform legal standard for methylmercury adulteration, and places the decision on what constitutes a safe level of methylmercury in the hands of agency experts, rather than the courts.

In this instance, rulemaking is a better method of regulation than case-by-case adjudication because methylmercury is a recurring substance in seafood and the dangers of exposure to methylmercury in the diet are scientifically documented. Rulemaking has been "increasingly substituted for adjudication as a regulatory technique, with the support and encouragement of courts, at least where the regulation involves specialized scientific knowledge."[53]

A regulatory limit would better serve the public interests in safe seafood and efficient government than does the present regulation by non-binding action level and court action under FDA's general enforcement authority.

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[52] National Nutritional Foods Association v. Weinberger, 512 F.2d 688, 698 (1975) (FDA has power to promulgate regulations for efficient enforcement of FFDCA).

[53] National Nutritional Foods Association, 512 F.2d at 698.

The FDA Has Authority to Set a Regulatory Limit for Methylmercury

The FDA has authority to set a regulatory limit for methylmercury under both the FFDCA and regulations limiting the quantity of an "added poisonous or deleterious substance" where that substance cannot be avoided by good manufacturing practice.[54]

There is no debate regarding the toxicity of mercury. The FDA first officially recognized methylmercury as a poisonous and deleterious substance in 1969, when it promulgated an action level for mercury in seafood.[55]

Mercury is an "added" substance in seafood, as that term has been defined by the courts.[56]

Mercury cannot be avoided by good manufacturing practices. There is no way of removing mercury from the oceans and it cannot be removed from seafood once it is caught.[57]

Under 21 C.F.R. § 109.6, a regulatory limit may be established when no technological or other changes are foreseeable in the near future that might affect the appropriateness of the limit established. There are no foreseeable technological or other changes in the ability to remove or avoid methylmercury that would affect the appropriateness of a regulatory limit set now. As long as fish

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[54] 21 C.F.R. § 109.4(b), § 109.6(c) (1991).

[55] 39 Fed. Reg. 42,738 (1974).

[56] U.S. v. Anderson Seafoods, Inc. at 1155.

[57] 39 Fed. Reg. 42,738 (1974).

are harvested from the waters, they will be contaminated by mercury which has been dumped there by industrial sources. Furthermore, the toxicity of methylmercury is sufficiently well-documented to set a regulatory limit that will protect pregnant women and children from methylmercury's adverse effects.

IV. THE FDA SHOULD CONSIDER THE ISSUE OF FETAL EFFECTS IN SETTING A REGULATORY LIMIT FOR METHYLMERCURY

The current action level is not adequate to protect the public health. In setting an action level, the federal government is implicitly guaranteeing that the food will be safe for general consumption by the population. Yet, the government has admitted that it failed to consider the potential effects on women of childbearing age and their offspring when it set the action level for mercury and the NAS had indicated concern about the adequacy of the current action level to protect babies and young children.

The risks of methylmercury exposure grow as consumers flock to seafood seeking lower fat sources of protein. Per capita consumption of seafood increased 24% between 1980 and 1990. Mercury-containing seafoods are very popular: swordfish and tuna are common menu items and canned tuna is likely the most commonly consumed form of seafood. In 1990, canned tuna accounted for 23.9% of all seafood consumed, according to the National Marine Fisheries Service.[58]

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[58] Telephone interview with Steve Koplin, National Marine Fisheries Service (Mar. 26, 1992).

The manner in which the current action level was set does not assure protection of large segments of the population. The groups of concern in this petition account for nearly half of the population: women of child-bearing age (15-44) account for 24% of the population and children age 14 and under are another 22%.[59]

The action level was set to protect a 70 kilogram (154 pound) man from overt effects. This action level may be considerably higher than the level necessary to protect women and children. The average weight for American women is 137.8 pounds and the average weight for a 10 year old child is 80.3 pounds.[60] Depending on their relative consumption, these groups may have greater exposure to methylmercury than that considered safe for men.

The studies documenting the special sensitivity of the fetus raise the specter that the current action level for methylmercury may have unanticipated effects on the next generation. For example, an increase in mental deficiency in the population, even at a rate lower than that found at Minamata, can result in substantial increases in the costs of education and in the productivity of the next generation.[61] Protecting the public

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[59] Telephone Interview with Population Information Staff, U.S. Bureau of the Census (Feb. 14, 1992). There are other groups that may be sensitive to exposure to mercury even at low doses, including the elderly and those suffering from malnutrition. These groups would probably bring the total at-risk population to over 50%.

[60] Telephone interview with Paula Summerour, National Center for Health Statistics (Feb. 18, 1992).

[61] Seafood Safety Symposium at 111.

health must include protecting the fetus from exposure to unsafe levels of toxins during development.

The FDA should initiate a rulemaking proceeding to set a regulatory limit for methylmercury that fully considers the potential effects of methylmercury exposure on the unborn, and on women and children, given present consumption patterns. Such consideration is clearly within the scope of FDA's mandate to protect the public health and it is essential to fulfill the mandate.

C. Environmental Impact

The action requested in this petition does not fall within the categories of actions requiring an environmental impact statement under 21 C.F.R. § 25.21 or an environmental assessment under 21 C.F.R. § 25.22. The action requested is of a type that does not individually or cumulatively have a significant effect on the human environment, as required under 21 C.F.R. § 25.23. The action is also subject to categorical exclusion under 21 C.F.R. § 25.24 because the regulatory limit "will not result in the introduction of any substance into the environment," but will limit the amounts of substances already being introduced.

D. Economic Impact

An economic impact statement under 21 C.F.R. § 10.30(b) is not required at this time.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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* Elizabeth Dahl, a third year law student at Georgetown University Law Center, provided invaluable assistance in the researching and writing of this petition.